Applicant: Howard Tucker Attorney's Docket No.: 06275-456US1 / 100889-1P US

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10/539106

JC17 Rec'd PCT/PTO 15 JUN 2005

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims:

1. (Currently amended) A compound of formula (I):

wherein

A is absent or is $(CH_2)_2$;

 R^1 is C_{1-8} alkyl, $C(O)NR^{10}R^{11}$, $C(O)_2R^{12}$, $NR^{13}C(O)R^{14}$, $NR^{15}C(O)NR^{16}R^{17}$, $NR^{18}C(O)_2R^{19}$, heterocyclyl, aryl or heteroaryl;

 R^{10} , R^{13} , R^{15} , R^{16} and R^{18} are hydrogen or C_{1-6} alkyl;

 R^{11} , R^{12} , R^{14} , R^{17} and R^{19} are C_{1-8} alkyl (optionally substituted by halo, hydroxy, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{3-6} cycloalkyl (optionally substituted by halo), C_{5-6} cycloalkenyl, $S(C_{1-4}$ alkyl), $S(O)(C_{1-4}$ alkyl), $S(O)(C_{1-4}$ alkyl), heteroaryl, aryl, heteroaryloxy or aryloxy), aryl, heteroaryl, C_{3-7} cycloalkyl (optionally substituted by halo or C_{1-4} alkyl), C_{4-7} cycloalkyl fused to a phenyl ring, C_{5-7} cycloalkenyl, or[[,]] heterocyclyl (itself optionally substituted by oxo, $C(O)(C_{1-6}$ alkyl), $S(O)_k(C_{1-6}$ alkyl), halo or C_{1-4} alkyl); or R^{11} , R^{12} , R^{14} and R^{17} can also be hydrogen;

or R^{10} and R^{11} , and/or R^{16} and R^{17} may join to form a 4-, 5- or 6-membered ring which optionally includes a nitrogen, oxygen or sulphur atom, said ring being optionally substituted by C_{1-6} alkyl, $S(O)_1(C_{1-6}$ alkyl) or $C(O)(C_{1-6}$ alkyl);

 R^2 is C_{1-6} alkyl, phenyl, heteroaryl or C_{3-7} cycloalkyl;

 R^3 is H or C_{1-4} alkyl;

R⁴ is aryl or heteroaryl; and

n is 2, 3 or 4;

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unless specified otherwise aryl, phenyl and heteroaryl moieties are independently optionally substituted by one or more of halo, cyano, nitro, hydroxy, $OC(O)NR^{20}R^{21}$, $NR^{22}R^{23}$, $NR^{24}C(O)R^{25}$, $NR^{26}C(O)NR^{27}R^{28}$, $S(O)_2NR^{29}R^{30}$, $NR^{31}S(O)_2R^{32}$, $C(O)NR^{33}R^{34}$, CO_2R^{36} , $NR^{37}CO_2R^{38}$, $S(O)_qR^{39}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy(C_{1-6})alkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, phenyl, phenyl(C_{1-4})alkyl, phenoxy, phenylthio, phenylS(O), phenylS(O)₂, phenyl(C_{1-4})alkoxy, heteroaryl, heteroaryl(C_{1-4})alkyl, heteroaryloxy or heteroaryl(C_{1-4})alkoxy; wherein any of the immediately foregoing phenyl and heteroaryl moieties are optionally substituted with halo, hydroxy, nitro, $S(C_{1-4}$ alkyl), $S(O)(C_{1-4}$ alkyl), $S(O)_2(C_{1-4}$ alkyl), $S(O)_2NH_2$, $S(O)_2NH(C_{1-4}$ alkyl), $S(O)_2N(C_{1-4}$ alkyl)₂, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, $C(O)NH_2$, $C(O)NH(C_{1-4}$ alkyl), $C(O)N(C_{1-4}$ alkyl)₂, CO_2H , $CO_2(C_{1-4}$ alkyl), $C(O)(C_{1-4}$ alkyl),

unless otherwise stated heterocyclyl is optionally substituted by C₁₋₆ alkyl [optionally substituted by phenyl {which itself optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, cyano, nitro, CF₃, OCF₃, (C₁₋₄ alkyl)C(O)NH, S(O)₂NH₂, C₁₋₄ alkylthio, S(O)(C₁₋₄ alkyl) or S(O)₂(C₁₋₄ alkyl)} or heteroaryl {which itself optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, cyano, nitro, CF₃, (C₁₋₄ alkyl)C(O)NH, S(O)₂NH₂, C₁₋₄ alkylthio, S(O)(C₁₋₄ alkyl) or S(O)₂(C₁₋₄ alkyl)}], phenyl {optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, cyano, nitro, CF₃, OCF₃, (C₁₋₄ alkyl)C(O)NH, S(O)₂NH₂, C₁₋₄ alkylthio, S(O)(C₁₋₄ alkyl) or S(O)₂(C₁₋₄ alkyl)}, heteroaryl {optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, cyano, nitro, CF₃, (C₁₋₄ alkyl)C(O)NH, S(O)₂NH₂, C₁₋₄ alkylthio, S(O)(C₁₋₄ alkyl) or S(O)₂(C₁₋₄ alkyl)}, S(O)₂NR⁴⁰R⁴¹, C(O)R⁴², C(O)₂(C₁₋₆ alkyl) (such as tert butoxycarbonyl), C(O)₂(phenyl(C₁₋₂ alkyl)) (such as benzyloxycarbonyl), C(O)NHR⁴³, S(O)₂R⁴⁴, NHS(O)₂NHR⁴⁵, NHC(O)R⁴⁶, NHC(O)NHR⁴⁷ or NHS(O)₂R⁴⁸, provided none of these last four substituents is linked to a ring nitrogen;

k, l, [[p]] and q are, independently, 0, 1 or 2;

 $R^{20},\,R^{22},\,R^{24},\,R^{26},\,R^{27},\,R^{29},\,R^{31},\,R^{33},\,R^{37} \text{ and } R^{40} \text{ are, independently, hydrogen or C_{1-6}}$ alkyl;

 R^{21} , R^{23} , R^{25} , R^{28} , R^{30} , R^{32} , R^{34} , R^{36} , R^{38} , R^{39} , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} , R^{47} and R^{48} are, independently, C_{1-6} alkyl (optionally substituted by halo, hydroxy, C_{1-6} alkoxy, C_{1-6} haloalkoxy,

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 C_{3-6} cycloalkyl, C_{5-6} cycloalkenyl, $S(C_{1-4}$ alkyl), $S(O)(C_{1-4}$ alkyl), $S(O)_2(C_{1-4}$ alkyl), heteroaryl, phenyl, heteroaryloxy or phenyloxy), C_{3-7} cycloalkyl, phenyl or heteroaryl; wherein any of the immediately foregoing phenyl and heteroaryl moieties are optionally substituted with halo, hydroxy, nitro, $S(C_{1-4}$ alkyl), $S(O)(C_{1-4}$ alkyl), $S(O)_2(C_{1-4}$ alkyl), $S(O)_2NH_2$, $S(O)_2NH(C_{1-4}$ alkyl), $S(O)_2N(C_{1-4}$ alkyl), $S(O)_2N(C_{1-4}$

 R^{21} , R^{23} , R^{25} , R^{28} , R^{30} , R^{34} , [[R^{35} ,]] R^{36} , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} and R^{47} may additionally be hydrogen;

or a pharmaceutically acceptable salt thereof or a solvate thereof.

- 2. (Original) A compound as claimed in claim 1 wherein A is absent.
- 3. (Currently amended) A compound as claimed in claim 1 [[or 2]] wherein n is 3.
- 4. (Currently amended) A compound as claimed in claim 1, [[2 or 3]] wherein R¹ is piperidin-1-yl or piperazin-1-yl 4-substituted by, or piperidin-4-yl 1-substituted by, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, phenyl {optionally substituted by, C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃ or OCF₃}, S(O)₂(C₁₋₄ alkyl), S(O)₂(C₁₋₄ fluoroalkyl), S(O)₂phenyl {optionally substituted by halo, cyano, C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃, OCF₃, S(O)₂(C₁₋₄ alkyl) or S(O)₂(C₁₋₄ fluoroalkyl)}, benzyl {optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃ or OCF₃}, C(O)H, C(O)(C₁₋₄ alkyl), benzoyl {optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃ or OCF₃}, C(O)₂(C₁₋₄ alkyl), C(O)NH₂, C(O)NH(C₁₋₄ alkyl) or C(O)NHphenyl {optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃ or OCF₃}.
- 5. (Currently amended) A compound as claimed in claim 1, $\frac{2}{7}$, $\frac{3}{9}$ or 4 wherein R^2 is phenyl optionally substituted by halo, C_{1-4} alkyl, C_{1-4} alkoxy, $S(O)_q(C_{1-4}$ alkyl), nitro, cyano or CF_3 ; wherein q is 0, 1 or 2.

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- 6. (Currently amended) A compound as claimed in any preceding claim $\underline{1}$ wherein R^3 is hydrogen.
- 7. (Currently amended) A compound as claimed in any preceding claim $\underline{1}$ wherein R^4 is phenyl optionally substituted by halo, C_{1-4} alkyl, C_{1-4} alkoxy, $S(O)_s(C_{1-4}$ alkyl), nitro, cyano or CF_3 ; wherein s is 0, 1 or 2.
- 8. (Original) A process for preparing a compound as claimed in claim 1, the process comprising
- a. when R¹ is an N-linked optionally substituted heterocycle, reacting a compound of formula (II):

$$R^2$$
 A
 A
 CI
 A
 A
 $CH_2)_n$
 $-R^4$
 (II)

wherein R², R³, R⁴, n and A are as defined in claim 1, with a compound R¹H (wherein the H is on a heterocycle ring nitrogen atom and R¹ is as defined in claim 1), in the presence of a suitable base, in a suitable solvent and, for example, at a room temperature; OR,

b. when R³ is hydrogen, coupling a compound of formula (III):

$$HN \rightarrow (CH_2)_n - R^4$$
 (III)

wherein R⁴, n and A are as defined in claim 1, with a compound of formula (IV):

$$R^2$$
 H O (IV)

wherein R^1 and R^2 are as defined in claim 1, in the presence of NaBH(OAc)₃ (wherein Ac is C(O)CH₃) in a suitable solvent at room temperature.

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9. (Original) A pharmaceutical composition which comprises a compound as claimed in claim 1, or a pharmaceutically acceptable salt thereof or solvate thereof, and a pharmaceutically acceptable adjuvant, diluent or carrier.

- 10. (Cancelled)
- 11. (Cancelled)
- 12. (Original) A method of treating a CCR5 mediated disease state comprising administering to a patient in need of such treatment an effective amount of a compound as claimed in claim 1, or a pharmaceutically acceptable salt thereof or solvate thereof.
 - 13. (New) A compound as claimed in claim 2, wherein n is 3.
- 14. (New) A compound as claimed in claim 2, wherein R^1 is piperidin-1-yl or piperazin-1-yl 4-substituted by, or piperidin-4-yl 1-substituted by, C_{1-6} alkyl, C_{3-7} cycloalkyl, phenyl {optionally substituted by, C_{1-4} alkyl, C_{1-4} alkoxy, CF_3 or OCF_3 }, $S(O)_2(C_{1-4}$ alkyl), $S(O)_2(C_{1-4}$ fluoroalkyl), $S(O)_2$ phenyl {optionally substituted by halo, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, CF_3 , OCF_3 .
- 15. (Currently amended) A compound as claimed in claim 2, wherein R^2 is phenyl optionally substituted by halo, C_{1-4} alkyl, C_{1-4} alkoxy, $S(O)_q(C_{1-4}$ alkyl), nitro, cyano or CF_3 ; wherein q is 0, 1 or 2.

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- 16. (New) A compound as claimed in claim 2, wherein R³ is hydrogen.
- 17. (New) A compound as claimed in claim 2, wherein R⁴ is phenyl optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, S(O)_s(C₁₋₄ alkyl), nitro, cyano or CF₃; wherein s is 0, 1 or 2.
- 18. (New) A compound as claimed in claim 3, wherein R¹ is piperidin-1-yl or piperazin-1-yl 4-substituted by, or piperidin-4-yl 1-substituted by, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, phenyl {optionally substituted by, C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃ or OCF₃}, S(O)₂(C₁₋₄ alkyl), S(O)₂(C₁₋₄ fluoroalkyl), S(O)₂phenyl {optionally substituted by halo, cyano, C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃, OCF₃, S(O)₂(C₁₋₄ alkyl) or S(O)₂(C₁₋₄ fluoroalkyl)}, benzyl {optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃ or OCF₃}, C(O)H, C(O)(C₁₋₄ alkyl), benzoyl {optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃ or OCF₃}, C(O)₂(C₁₋₄ alkyl), C(O)NH₂, C(O)NH(C₁₋₄ alkyl) or C(O)NHphenyl {optionally substituted by halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃ or OCF₃}.
- 19. (New) A compound as claimed in claim 3, wherein R^2 is phenyl optionally substituted by halo, C_{1-4} alkyl, C_{1-4} alkoxy, $S(O)_q(C_{1-4}$ alkyl), nitro, cyano or CF_3 ; wherein q is 0, 1 or 2.
 - 20. (New) A compound as claimed in claim 3, wherein R³ is hydrogen.
- 21. (New) A compound as claimed in claim 3, wherein R^4 is phenyl optionally substituted by halo, C_{1-4} alkyl, C_{1-4} alkoxy, $S(O)_s(C_{1-4}$ alkyl), nitro, cyano or CF_3 ; wherein s is 0, 1 or 2.